

How to develop smarter host mixtures to control plant disease?

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Abstract

A looming challenge for agriculture is sustainable intensification of food production to feed the growing human population. Current chemical and genetic technologies used to manage plant diseases are highly vulnerable to pathogen evolution and are not sustainable. Pathogen evolution is facilitated by the genetic uniformity underlying modern agroecosystems, suggesting that one path to sustainable disease control lies through increasing genetic diversity at the field scale by using genetically diverse host mixtures. We investigate how host mixtures can improve disease control using a population dynamics model. We find that when a population of crop plants is exposed to host-specialized pathogen species or strains, the overall disease severity is smaller in the mixture of two host varieties than in each of the corresponding pure stands. The disease severity can be minimized over a range of mixing ratios. These findings may help in designing host mixtures that efficiently control diseases of crops. We then generalize the model to describe host mixtures with many components. We find that when pathogens exhibit host specialization, the overall disease severity decreases with the number of components in the mixture. Using these model outcomes, we propose ways to optimize the use of host mixtures to decrease disease in agroecosystems.

1. Introduction

Growing demand for higher quality food coupled with global population growth led the Food and Agriculture Organization of the United Nations to predict that food production will need to increase by 70 % by 2050 [1]. This increase can be achieved by expanding growing areas (extensification) or by increasing yields per hectare (intensification). Either approach will increase the overall biomass of crop plants and thus raise the carrying capacity of agricultural plant pathogens. Increasing international travel and trade exposes crops to many new pathogens, which contributes to the emergence of new diseases. As a result of these developments, crops will become more vulnerable to infectious diseases that cause damaging epidemics and substantially reduce yields [2].

The two most widely used disease control measures are applications of chemicals (fungicides and antibiotics) and breeding for disease resistant crop cultivars by incorporating resistance genes. Both of these control measures are highly vulnerable to pathogen adaptation. Many pathogens have repeatedly evolved to overcome resistance conferred by major resistance genes (reviewed in [3, 4]). A recent example is the emergence of virulent races of stem rust (called Ug99) that can infect about 90 % of wheat varieties grown worldwide [5]. Similarly, many fungicides rapidly lose their efficacy because of the emergence and fixation of mutations encoding fungicide resistance (e.g. [6, 7]). An important disadvantage of fungicides relative to genetic resistance is their high cost and harmful effects on the environment. As a result of pathogen evolution, the current commonly practiced disease control measures will likely be inadequate to enable a sustainable intensification of food production.

Quantitative or partial resistance is thought to be more durable [4, 8], but has not been as widely utilized as major gene resistance. Recent research has begun to provide insights into the molecular mechanisms responsible for quantitative resistance [9, 10], but studies that include quantitative resistance in epidemiological models are rare (Lo Iacono et al., 2012). Pathogens can still adapt to quantitative resistance leading to an erosion of its effects [11, 12, 3, 13], although at a much slower pace compared to major resistance genes.

More effective and longer-lasting disease control methods are urgently needed to achieve a sustainable intensification of crop production. One way to develop such methods is to focus on the underlying properties of modern agricultural ecosystems (agroecosystems) that make them vulnerable to plant pathogens. Compared to natural ecosystems, agroecosystems are more environmentally homogeneous, have a higher density of plants, and possess much less genetic and species diversity. Increasing the environmental and genetic homogeneity of agroecosystems enabled a high degree of mechanization and contributed greatly to the efficiency of food production and the development of food processing industries. But these developments also favored the emergence of new pathogens with higher virulence and a greater degree of host specialization [14] and accelerated the evolution of existing pathogens towards higher virulence [15, 16]. It is increasingly recognized that these underlying properties of agroecosystems, especially the lack of genetic diversity due to the dominance of monoculture crops grown as clones, make them especially susceptible to disease epidemics [17, 18, 19].

For these reasons, many researchers propose to deliberately increase genetic diversity in agroecosystems [15, 20, 21] in order to decrease disease in the short-term and enhance the durability of disease resistance in the long-term. This diversity can be created within a single genetic background by developing multiline cultivars [22] or involve many genetic backgrounds by using variety mixtures [23, 24, 17]. Because they are based on a single, uniform genetic background, multilines offer the advantage of a more homogeneous crop that is more amenable to highly mechanized industrial farming and food processing. But the disadvantage of multilines is that it takes many years of backcrossing to create a multiline variety, and the resulting multiline is unlikely to possess the best yield or quality characteristics for all local environments. But progress in genetic engineering of plants is likely to lead to the development of resistance gene cassettes [25, 15] that can enable the rapid synthesis of locally adapted multiline cultivars that carry an assortment of different resistance genes, combining the resistance gene diversity useful for controlling diseases with the background crop genotype uniformity useful for efficient food production and processing. In this study the distinction between multiline cultivars and variety mixtures is not important, so we will refer to both options simply as host mixtures.

Many field experiments have been performed to determine whether host mixtures reduce the amount of fungal disease on crop plants (e.g. [26, 27, 28, 29, 21, 30, 31, 32], see also reviews [33, 17, 34, 24, 23] and references therein). The findings of over 30 studies (mostly in barley, wheat, rice and beans) were summarized in [24]. The vast majority of experiments showed less disease in mixtures as compared to the mean of the pure stands for obligate pathogens such as rusts and mildews. However, there was a large variation in the percentage of disease reduction: for example, between 9 % and 80 % for powdery mildew in barley, and between 13 % and 97 % for stripe rust in wheat. A recent meta-analysis of stripe rust on wheat considered 161 mixture cases reported in 11 publications [26]. In 83 % of these cases the average disease level was found to be lower in mixtures compared to the mean of the pure stands. A reduction in disease of between 30 % and 50 % was found most frequently. A large-scale study performed in China demonstrated that row mixtures of rice varieties could strongly reduce rice blast [21]. Thus, host mixtures reduce the amount of disease in most studied cases, but the outcomes exhibit a wide variation, even within a single study (for example [29]).

This variation is one of the reasons why multilines and cultivar mixtures have so far gained little acceptance among seed companies or growers. To achieve reliable disease control, we need to identify the conditions under which mixtures work best and use this knowledge to design optimal mixtures. This requires a better understanding of the underlying mechanisms of disease reduction in mixtures. Our study contributes to this understanding in three important ways by using a population dynamics model of plant-pathogen interactions. First, we identified conditions where mixtures are superior compared to pure stands. Second, we defined optimal ratios of components to include in the mixture. Third, we determined optimal numbers of components to include in the mixture.

This was done by exploring possible disease outcomes when two or more hosts are mixed in the presence of two or more pathogen strains or species. This approach is a substantial advance with respect to previous modeling studies that mostly concentrated

on a single pathogen strain [35, 36, 19, 37, 38] with the exception of a few studies that considered several pathogen genotypes (e. g. [39, 40, 41]). It is crucial to consider more than one pathogen in the model, because practically all fields are colonized by more than one pathogen strain and several pathogen species and the full advantage of host mixtures manifests in reduction of the overall pathogen load. Moreover, we obtained analytical solutions that allowed us to investigate the disease reduction over the whole range of parameters that includes both qualitative and quantitative host resistance (see Sec. 3).

2. Model and assumptions

We first consider the case when two host varieties H_1 and H_2 are exposed to two types of pathogen: 1 and 2 (we also refer to them as P_1 and P_2). These could be either different strains (races or pathotypes) of the same pathogen or different pathogen species capable of infecting the same host tissue. To describe the host-pathogen interaction, we use a deterministic epidemiological model of susceptible-infected dynamics (see Fig. 1), which is an extension of the model described previously [42] to the case of two different hosts. This model can be applied to a variety of aerially and splash-dispersed, polycyclic pathogens of cereal crops, such as the fungi and bacteria causing rusts, mildews, blasts, spots and blotches.

$$\frac{dH_1}{dt} = r(K_1 - H_1) - (\beta_{11}I_1 + \beta_{21}I_2)H_1, \quad (1)$$

$$\frac{dH_2}{dt} = r(K_2 - H_2) - (\beta_{12}I_1 + \beta_{22}I_2)H_2, \quad (2)$$

$$\frac{dI_1}{dt} = (\beta_{11}H_1 + \beta_{12}H_2)I_1 - \mu I_1, \quad (3)$$

$$\frac{dI_2}{dt} = (\beta_{21}H_1 + \beta_{22}H_2)I_2 - \mu I_2. \quad (4)$$

There are four compartments in the model: susceptible hosts H_1 of variety 1, susceptible hosts H_2 of variety 2, hosts I_1 infected by pathogen 1 and hosts I_2 infected by pathogen 2. Each of the quantities H_1 , H_2 , I_1 , I_2 represents the total amount of the corresponding host tissue within one field, which could be leaves, stems or grain tissue, depending on the host-pathogen combination.

Susceptible hosts H_1 and H_2 grow with the same rate r . Their growth is limited by their “carrying capacities” K_1 and K_2 , implying limitations in space or nutrients. One can vary the proportion of host plants of the two varieties by adjusting the ratio of the corresponding seeds to be planted. This is reflected in the change of the ratio $\phi_1 = K_1/(K_1 + K_2)$ in the model. We assume that the seeds of the two host varieties are well mixed before planting, such that the spatial distribution across the field is uniformly random for both types of plants. The infected host tissue loses its infectivity (i. e. the ability to produce infectious spores) with the rate μ (μ^{-1} is the average infectious period), which is assumed to be the same for I_1 and I_2 .

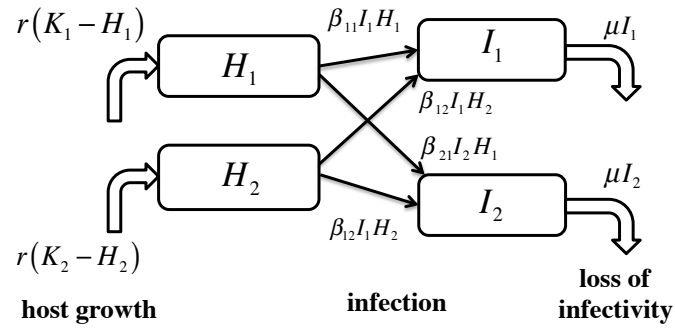


Figure 1: Scheme of the model equations (1)-(4).

| | H₁ | H₂ |
|----------------------|----------------------|----------------------|
| P₁ | $\beta_{11} \quad +$ | $\beta_{12} \quad -$ |
| P₂ | $\beta_{21} \quad +$ | $\beta_{22} \quad +$ |

Figure 2: Scheme of the host-pathogen interaction. “+”, “-” signs correspond to a “pure” gene-for-gene (GFG) interaction. The transmission matrix β_{ij} , $i, j = 1, 2$ represents a more general description with “pure” GFG ($\beta_{11} = \beta_{22} = \beta_{21} > 0$; $\beta_{12} = 0$) and full host specialization ($\beta_{11}, \beta_{22} > 0$; $\beta_{12} = \beta_{21} = 0$) as limiting cases.

We assume that the two host varieties differ only in their susceptibility to the two pathogens, and the two pathogens differ only in their capability to infect the two hosts, which is reflected in the rate of spore production and the ability of resulting spores to infect additional host tissue. Both host susceptibility and pathogen virulence are described in the model by the four transmission rates β_{11} , β_{22} , β_{12} , and β_{21} . They can be conveniently arranged in a transmission matrix or WAIFW (Who Acquires Infection From Whom) matrix

$$\mathbf{B} = \begin{vmatrix} \beta_{11} & \beta_{12} \\ \beta_{21} & \beta_{22} \end{vmatrix}. \quad (5)$$

The first index of matrix elements represents the source of infection and the second index represents the recipient of infection (see Fig. 2). For example, β_{12} describes the transmission rate from I_1 to H_2 . Possible relationships between the elements of the transmission matrix are discussed in Section 3. We neglected spatial dependence of pathogen dispersal: every infected host is equally likely to infect every other infected host within the population (often called the “mass-action” approximation). This approximation is valid for air-borne pathogens with long-range dispersal (for example, rusts and mildews) and for sufficiently small plot sizes.

Note that I_1 includes the tissue of both hosts infected by pathogen 1. Similarly, I_2 includes host tissue of both hosts infected by the pathogen 2. This formulation assumes that the transmission rate does not depend on the host variety of the source of infection, but only depends on the host variety of the recipient of infection. In other words, under this assumption, the spore production rate and the quality of spores produced depend on the pathogen genotype, but not on the host genotype. But the infection efficiency (or infection success) of a spore depends on the host genotype on which it lands. In order to relax this assumption, one needs to subdivide each of I_1 and I_2 into two compartments, according to the type of host tissue infected.

In order to quantify the amount of disease, we use the proportion of infected area of the host tissue

$$y = (I_1 + I_2)/(I_1 + I_2 + H_1 + H_2), \quad (6)$$

and call it *disease severity*. We will often use the equilibrium values of y , I_1 , I_2 , H_1 , H_2 (denoted by an “*”-superscript), which are achieved over long periods of time. They correspond to the stable fixed point of the system (1)-(4), as explained in the Appendix A.1 and A.2.

We will also consider a more general case of a mixture with n hosts that is exposed to n pathogens. In this case, the dynamics of the host-pathogen interactions are described by this system of $2n$ equations that is a generalization of the system of Eqs. (1)-(4):

$$\frac{dH_i}{dt} = r(K_i - H_i) - \sum_{k=1}^n \beta_{ki} I_k H_i, \quad (7)$$

$$\frac{dI_i}{dt} = \sum_{k=1}^n \beta_{ik} I_i H_k - \mu I_i, \quad i = 1, \dots, n \quad (8)$$

Here, the transmission matrix \mathbf{B} is an $n \times n$ square matrix, the element β_{ik} describes the transmission rate of the pathogen that originates from the infected host of type i and infects the healthy host of variety k . We assume that every host variety is planted at the same proportion, i. e. $K_i = K$.

We will vary the number of host varieties in the mixture n , while keeping the total carrying capacity constant: $K_{\text{tot}} = \sum_{i=1}^n K_i = nK$. We will consider the total amount of healthy and infected hosts at the infected equilibrium of the system of Eqs. (7)-(8)

$$H_{\text{tot}}^* = \sum_{i=1}^n H_i^*, \quad I_{\text{tot}}^* = \sum_{i=1}^n I_i^*. \quad (9)$$

and the total disease severity defined by

$$y_{\text{tot}}^* = \frac{I_{\text{tot}}^*}{I_{\text{tot}}^* + H_{\text{tot}}^*}. \quad (10)$$

In order to obtain an analytical solution for the disease severity Eq. (10), we consider the transmission matrix of a simple form

$$\mathbf{B} = \begin{pmatrix} \beta_d & \beta_{\text{nd}} & \cdots & \beta_{\text{nd}} \\ \beta_{\text{nd}} & \beta_d & \cdots & \beta_{\text{nd}} \\ \vdots & & \ddots & \\ \beta_{\text{nd}} & \cdots & & \beta_d \end{pmatrix} \quad (11)$$

Here, every diagonal element of the matrix \mathbf{B} is equal to β_d and every non-diagonal element is β_{nd} . We generally assume partial specialization, where $\beta_d \geq \beta_{\text{nd}}$. Furthermore, assuming that all healthy and infected hosts start with the same initial conditions, their

dynamics will be the same. Hence, $H_i = H_p$, $I_i = I_p$ for any i and we can simplify the Eqs. (7)-(8):

$$\frac{dH_p}{dt} = r(K - H_p) - \beta_{\text{eff}} I_p H_p, \quad (12)$$

$$\frac{dI_p}{dt} = \beta_{\text{eff}} I_p H_p - \mu I_p, \quad (13)$$

where $\beta_{\text{eff}} = \beta_d + (n - 1)\beta_{\text{nd}}$.

3. Possible relationships between transmission rates

What are the possible relationships between the transmission rates β_{ij} , $i, j = 1, 2$? The answer requires an understanding of the host-pathogen interaction on the molecular level [43, 44]. Our current knowledge can be summarized in a simplified way using a four-stage model [45, 43, 44]. First, plants have a basal (or innate) immune system. It consists of pathogen recognition proteins (PRPs) that respond to microbe-associated molecular patterns (MAMPs, also called pathogen-associated molecular patterns or PAMPs). MAMPs are typically highly conserved molecules produced by pathogens, for example chitin in fungi or flagellin in bacteria. Upon MAMP recognition, PRPs activate basal immune responses and the infection is prevented. Second, pathogens evolve to suppress the basal immune responses by producing multiple effector proteins (E-proteins or effectors), which target host proteins and suppress host resistance. Third, plant resistance genes (R-genes) produce NB-LRR proteins (R-proteins), which recognize the effector proteins of the pathogen and restore resistance. Finally, pathogens avoid recognition by modifying or removing the effector proteins. As a result, the R-proteins can no longer recognize the effector proteins and resistance is lost again. Thus loss or modification of effector proteins is expected to confer a fitness cost to pathogens, since they can be essential for pathogenicity in the second step described above. Loss of some effectors (called “core effectors”) confers a sizable fitness cost. These effectors can be identified using a combination of genetic and genomic methods [45].

Next, we discuss how different possibilities of host-pathogen interaction on the molecular level affect the relationship between the elements of the transmission matrix B . First, assume that only one combination of an R-protein and an E-protein determines the values of the transmission matrix. Consider the case when host 1 has the R-protein, while host 2 does not have it; and pathogen 1 has the corresponding E-protein, while pathogen 2 does not have it. In this case, the interaction follows the “pure” GFG scheme, i.e. $\beta_{11} = \beta_{22} = \beta_{21} > 0$, $\beta_{12} = 0$ (see Fig. 2), provided that elimination the E-protein does not affect pathogen fitness and the presence of the R-gene does not confer a fitness cost to the host. We denote this scenario as (A). If the loss or mutation of an effector confers a fitness cost, then $\beta_{11} > \beta_{21}$. Thus, we obtain $\beta_{11} > \beta_{22} = \beta_{21} > 0$, $\beta_{12} = 0$ and denote this scenario as (B). In the case when the presence of an R-protein confers a fitness cost to the host that manifests in an increased susceptibility to the pathogen P_2 , then we have the relationship $\beta_{11} > \beta_{22} > \beta_{21} > 0$, $\beta_{12} = 0$, and call it scenario (C).

The three scenarios considered above result from an interaction of a single R-protein – E-protein pair (R–E pair), but in reality there are many R-proteins and many E-proteins [43], which can be active in the same host-pathogen combination. Effects of these multiple interactions on the host susceptibility to disease are expected to sum up [43]. Under the GFG scheme [scenario (A) above], their combined effect may manifest as a “pure” GFG. Alternatively, it can manifest as an interaction with a quantitative degree of specialization. This can occur when some of the R-proteins are present in host 1, but absent in host 2 and vice versa, and, similarly, some of E-proteins are present in pathogen 1, but absent in pathogen 2 and vice versa.

To better understand this, consider the simplest example when there are only two R–E pairs, R1–E1 and R2–E2, where R1 only recognizes E1 and R2 only recognizes E2. Complete resistance occurs when both recognition events occur, i.e. when the host has both R1 and R2 and the pathogen has both E1 and E2. Consider the case when each pathogen has one of the effectors, but lacks the other one; and each host has one of the R proteins, but lacks the other one. For example, pathogen 1 has E1, but lacks E2, while pathogen 2 has E2, but lacks E1. Similarly, host 1 has R2, but lacks R1, while host 2 has R1, but lacks the R2. In this case, the infection of host 2 by pathogen 1 (transmission rate β_{12}) is suppressed by the recognition of the protein E1 by the protein R1. Here, only one of the two possible R–E recognitions occur, consequently the resistance is incomplete. The same happens when host 1 is attacked by pathogen 2 (rate β_{21}). In the other two possibilities, when pathogen 1 attacks host 1, or pathogen 2 attacks host 2, we expect full susceptibility, since R–E recognition is absent. Thus, pathogen 1 specializes on host 1, and pathogen 2 specializes on host 2, but the degree of specialization is incomplete, since the cross-transmission rates are still positive. This scenario [we will call it (D)] corresponds to both diagonal elements of the transmission matrix being larger than both non-diagonal ones, i.e. $\beta_{11}, \beta_{22} > \beta_{21}, \beta_{12} > 0$.

Moreover, if we allow for further deviations from the “pure” GFG scheme due to fitness costs of losing effectors for pathogens and also costs of having “unnecessary” R-proteins for hosts, then many more outcomes become possible and we are even more likely to find pairs of pathogens and hosts which exhibit a degree of specialization [i.e. interact via scenario (D) discussed above].

As we have seen above, the variety of possible outcomes for the transmission matrix \mathbf{B} is already quite large even when considering only two R-proteins and two E-proteins. For larger numbers of R- and E-proteins, we expect the transmission matrix \mathbf{B} to exhibit even richer behavior. Therefore, it is desirable to study the benefit of mixing host varieties representing the whole range of values of the matrix elements of \mathbf{B} . We have done this by obtaining analytical expressions for the disease severity and frequencies of pathogens as functions of the matrix elements β_{ij} and other model parameters (see Appendix A.1). This is an advantage of our study with compared to previous theoretical investigations that assumed a “pure GFG” interaction, without fitness costs associated with losing effectors [46, 47, 48], or that assumed full specialization [40], where each pathogen can only infect its preferred host and is unable to infect any other hosts (also called the “matching alleles” model [49]). The latter scenario seems to represent only a hypothetical limiting case, because it requires full resistance, which is unlikely given

the simultaneous presence of many pairs of R- and E-proteins. In contrast, partial specialization (scenario (D)), when the diagonal elements β_{11} and β_{22} are larger than non-diagonal ones β_{12} and β_{21} , but the non-diagonal ones are still significantly larger than zero, seems to be the most generic case. This is because it arises from a ubiquitous GFG-type of interaction with many R-proteins present in the host, many corresponding E-proteins present in the pathogen, as well as fitness costs for the pathogen due to elimination or modification of E-proteins and fitness costs for the host due to having unnecessary R-proteins.

Our conclusion that partial specialization is quite common, if not universal in plant-pathogen interaction is confirmed by the findings of several artificial selection experiments [50, 32, 51, 52, 53], where pathogen strains were observed that are better adapted to particular host cultivars than to other cultivars (differential adaptation). In several cases, quantitative resistances were identified in these host cultivars [13, 54]. Also, cross-inoculation studies with field isolates demonstrate that pathogen strains are often better adapted to cultivars from which they were isolated [55, 56]. [See [57] p.417-419 for a detailed discussion]. Moreover, local adaptation of pathogens to their hosts was detected in studies of wild plant-pathogen systems (e. g. *Linum marginale*–*Melampsora lini* [58], *Plantago lanceolata*–*Podosphaera plantaginis* [59]).

4. Results

We first consider the effect of host mixtures on the competition between the two pathogen strains (Sec. 4.1). Then, in Sec. 4.2 we determine what proportions of hosts in the mixture will minimize the disease. Finally, we generalize our approach to the case of many pathogen strains and host varieties and determine an optimal number of components in a host mixture (Sec. 4.3).

4.1. Long-term outcomes of the host-pathogen dynamics

Understanding long-term outcomes is crucial to determine whether a host mixture will reduce the amount of disease. Moreover, long-term outcomes are simple to determine, because they correspond to stability ranges of the fixed points of the system of Eqs. (1)–(4) and can be found analytically (see Appendix A.1 and A.2).

The case when the two host varieties have the same susceptibility to disease, $\beta_{11} = \beta_{12} = \beta_1$, $\beta_{22} = \beta_{21} = \beta_2$ is equivalent to having just one host variety. In this case, the long-term outcome depends on the basic reproductive numbers of the two pathogens: $R_{01} = \beta_1 K_1 / \mu$ and $R_{02} = \beta_2 K_2 / \mu$. If both $R_{01} < 1$ and $R_{02} < 1$, then both pathogens die out [gray region in Fig. 3(a)]. If at least one of the R_0 's exceeds unity, then the pathogen with the larger R_0 survives and the pathogen with the smaller R_0 dies out, and no stable co-existence is possible, as shown by red and blue regions in Fig. 3(a).

In contrast, when the two host varieties differ in their susceptibility to disease, stable co-existence of the two pathogens becomes possible. This is realized when each of the pathogens at least partially specializes on one of the hosts, i. e. $\beta_{11}, \beta_{22} > \beta_{21}, \beta_{12}$

[scenario (D) discussed in Sec. 2]. Now, the diagram of outcomes looks different [cf. Fig. 3(a) and (b)]: the regions of domination of P_1 and P_2 are now separated by a broad region, where P_1 and P_2 exhibit stable co-existence.

The vertical dashed line indicates the threshold value $\beta_{22} = \beta_{22c}$ [Eq. (A.25)], above which pathogen 1 can invade the host population in the absence of pathogen 2. Similarly, the horizontal dashed line shows the invasion threshold $\beta_{11} = \beta_{11c}$ [Eq. (A.29)] of pathogen 2 in the absence of pathogen 1. Hence, in the lower left region of the graph, separated by these two lines, neither pathogen can invade and therefore they die out.

At $\beta_{11} > \beta_{11c}$ pathogen 1 can invade the host population in the absence of pathogen 2. Assume that this has happened and pathogen 1 has reached equilibrium with the host population. Note that the threshold value of β_{22} , above which pathogen 2 can also invade is larger than in the absence of pathogen 1. This is because pathogen 1 has occupied some of the healthy host tissue, and since the basic reproductive number is proportional to the amount of healthy host tissue, the threshold value β_{22c} increases. Thus, if there is a degree of specialization of the pathogens with respect to their hosts (i. e. $\beta_{11}, \beta_{22} > \beta_{12}, \beta_{21}$), then the stable coexistence of the two pathogens is possible.

4.2. Is there an optimal mixture of host varieties?

Planting a mixture of host varieties provides an additional parameter that can be adjusted, namely the proportions of the varieties in the mixture. Does planting a mixture of hosts reduce the total amount of disease compared to the case of monoculture stands? Furthermore, is there an optimal proportion of the host varieties at which the amount of disease is minimized? Answers to these questions depend on the relationships between the elements of the transmission matrix \mathbf{B} .

We calculate the disease severity at equilibrium y^* [Eq. (A.16)] as a function of the proportion of the host variety 1 in the mixture $\phi_1 = K_1/K$ [see Fig. 4(a)]. The quantity ϕ_1 is varied from zero to one, while keeping the total carrying capacity of hosts $K = K_1 + K_2$ constant.

When each pathogen can infect both hosts equally well (i. e. $\beta_{12} = \beta_{11}, \beta_{21} = \beta_{22}$, no specialization), disease severity does not depend on ϕ_1 [black dashed curve in Fig. 4(a)]. The same outcome is observed when the host-pathogen interaction strictly follows the gene-for-gene scheme, i. e. $\beta_{21} = \beta_{22} > \beta_{11} > 0, \beta_{12} = 0$ [yellow dashed curve in Fig. 4(a)]. We used the values of the transmission rates, which satisfy $\beta_{22} > \beta_{11}$. Hence, pathogen 2 is fitter than pathogen 1 and dominates the population and at any value of ϕ_1 [black and yellow dashed curve in Fig. 4(b)].

In the case of a single pathogen infecting a mixture of hosts with different degrees of susceptibility ($\beta_{22} = \beta_{12} > \beta_{11} = \beta_{21}$), the disease severity decreases linearly with ϕ_1 . In this case, simply using a monoculture with the more disease-resistant host variety ($\phi_1 = 1$) would reduce the disease most strongly [green dashed-dotted curve in Fig. 4(a)]. This is in agreement with findings of an experiment, in which a mixture of a susceptible and resistant barley variety was infected by barley powdery mildew (caused by *Blumeria graminis* f. sp. *hordei*) reported in [34]. In this study the disease reduction was found to decrease linearly with the proportion of the susceptible variety in the mixture.

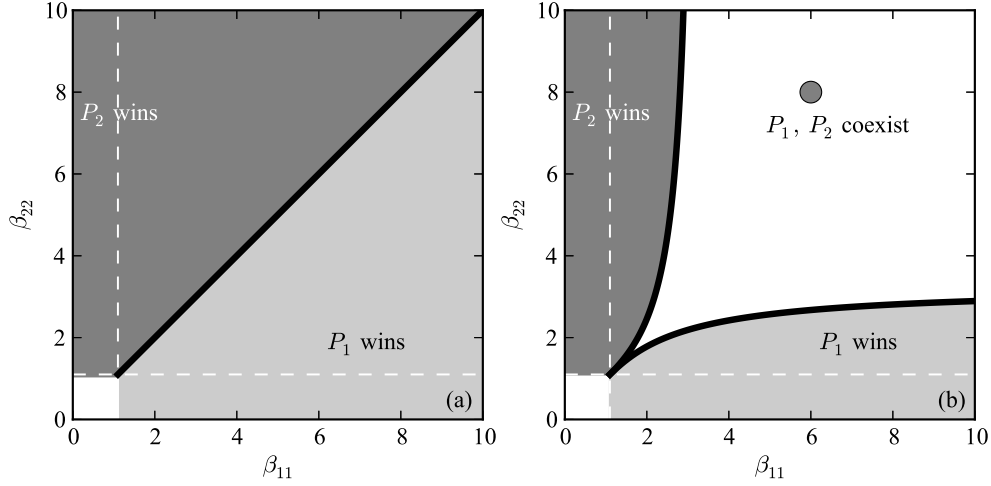


Figure 3: Long-term outcomes of the host-pathogen dynamics described by Eqs. (1)-(4) versus the transmission rates β_{11} and β_{22} . Panel (a): both host varieties have the same susceptibility, i. e. $\beta_{11} = \beta_{12} = \beta_1$, $\beta_{22} = \beta_{21} = \beta_2$; panel (b): the two host varieties differ in their susceptibility (β_{11} and β_{22} are varied, while $\beta_{12} = 0.9$, $\beta_{21} = 0.9$). Possible outcomes correspond to different fixed points of Eqs. (1)-(4) and their ranges coincide with the ranges of stability of the fixed points (see Appendix A.1 and A.2). They are shown in different shades of grey: (i) both pathogens P_1 and P_2 die out (white rectangle in the lower left corner); (ii) P_1 survives, P_2 dies out (dark grey); (iii) P_2 survives, P_1 dies out (light grey); (iv) P_1 and P_2 coexist (white). Solid black curves in (b) are plotted according to Eq. (A.29) and Eq. (A.25). Parameter values: $K_1 = K_2 = 0.5$, $\mu = 1$. Grey circle corresponds to same parameter values as dashed vertical lines in Fig. 4.

The picture changes if there is a degree of specialization of pathogen strains or species to host varieties ($\beta_{22}, \beta_{11} > \beta_{12}, \beta_{21}$). In this case the disease severity y^* first decreases with ϕ_1 , then reaches a constant value, and after that increases again. Thus, the disease is reduced over a range of intermediate values of ϕ_1 (solid red and blue curves). The magnitude of this reduction increases with the degree of specialization and reaches a maximal value at full specialization (solid red curve). Also, the range of ϕ_1 -values, over which the proportion of disease remains minimal, increases with the degree of specialization [cf. blue and red curves in Fig. 4(a)].

The ranges over which the frequency of pathogen 2 remains constant or changes as a function of the cropping ratio ϕ_1 correspond to the ranges of stability of different fixed points of the model system Eqs. (1)-(4). This can be seen from Fig. 4(b), where the frequency f_2 of pathogen 2 is shown versus ϕ_1 . In the region where y^* decreases with ϕ_1 , pathogen 2 dominates the population ($f_2 = 1$). In the region where y^* stays constant, the two pathogens co-exist, but the frequency of pathogen 2 decreases with ϕ_1 until it reaches zero. This occurs at the border, where another fixed point becomes stable, the one corresponding to pathogen 1 dominating the population ($f_2 = 0$). Here, the disease severity increases with ϕ_1 .

Why does the disease severity decrease with ϕ_1 at small values of ϕ_1 ? In this parameter range, pathogen 2 dominates the population in the long term. Since pathogen 2 specializes on host 2, it develops best when only host 2 is planted, i.e. at $\phi_1 = 0$. By adding a small amount of host 1 to the mixture, we create suboptimal conditions for pathogen 2: it is still able to outcompete pathogen 1, but since there is less of its preferred host tissue, the resulting disease severity is smaller. A similar explanation holds for the increase of disease severity with ϕ_1 at large values of ϕ_1 .

Why does the disease severity stay constant over a range of intermediate values of ϕ_1 ? This range corresponds to co-existence of the two pathogens. Since there is a degree of specialization, by increasing ϕ_1 we make pathogen 1 more fit while pathogen 2 becomes less fit. These two changes compensate each other, so that the total disease severity, which includes both pathogen strains, remains the same.

When the pathogen-host specialization is not complete ($\beta_{21} > 0, \beta_{12} > 0$) and the two pathogens coexist (at intermediate values of ϕ_1), the two pathogens compete with each other for host tissue. The effect of this competition on the amount of disease is illustrated in Fig. 5: panel (a) shows the amount of host tissue I_1^* infected by P_1 versus ϕ_1 , when P_2 is present (blue, solid curve) and absent (red, dashed curve). The presence of P_2 decreases I_1^* across almost the whole range of ϕ_1 , except for the largest values, where P_1 dominates the population and P_2 dies out. However, if we look at the overall disease severity caused by both pathogens [Fig. 5(b)], the presence of P_2 makes it larger. Therefore, although the application of P_2 as a biocontrol measure suppresses P_1 , it also increases the overall disease severity. This could only be considered as a reasonable control measure, if pathogen P_1 is much less desirable (e.g. it produces a mycotoxin that is not produced by P_2 or has a higher risk of developing fungicide resistance compared to P_2), while a certain degree of infection with P_2 can still be tolerated.

A prominent example where this model can be applied in the context of biocontrol is illustrated with *Aspergillus flavus*, a fungal pathogen that can infect a variety of crops,

including maize, cottonseed, peanuts, and tree nuts. Some strains of *A. flavus* produce aflatoxins, toxic carcinogenic fungal metabolites that contaminate food (aflatoxigenic strains), while others do not (atoxigenic strains). Atoxigenic strains are deliberately applied to crops as a form of biocontrol to mitigate aflatoxin contamination [60]. In the example case considered in Fig. 5, when the atoxigenic strain P_2 is applied, it may outcompete the aflatoxigenic strain P_1 , leading to its eradication. Our model predicts that this occurs at a low enough proportion of the host variety H_1 in the mixture (i. e. the cropping ratio ϕ_1 should be below a certain value marked by a vertical dotted line in Fig. 5).

Thus, mixing host varieties reduces the overall disease severity if each of the pathogens performs better on its preferred host. In this case, an optimal proportion of host varieties in the mixture lies in the intermediate range, over which the two pathogens exhibit stable co-existence. This result is in agreement with previous theoretical studies [40] and also explains some experimental findings [53].

In addition, within the range of maximal overall suppression of disease, the ratio of the two pathogens can be controlled by varying the proportion of hosts in the mixture [Fig. 4(a) and (b)]. This can be useful, if one of the pathogens is much less desirable, for example, because of mycotoxin production or the risk of fungicide resistance.

4.3. What is the optimal number of components to use in a host mixture?

So far we considered a host mixture with only two components. Does adding more components to the mixture lead to better disease control? We use the mathematical framework of Eqs. (12)-(13) to address this question. In the simplified case of partial specialization all elements of the transmission matrix \mathbf{B} are positive. All the diagonal elements are equal to β_d and the non-diagonal ones are equal to β_{nd} , with $\beta_d > \beta_{nd} > 0$ (see Eq. (11)). In this case, we determined the analytical expression for the total disease severity at the infected equilibrium

$$y_{\text{tot}}^*(n) = r \frac{(\beta_d + (n-1)\beta_{nd}) K_{\text{tot}} - \mu n}{n\mu(\mu - r) + rK_{\text{tot}}(\beta_d + (n-1)\beta_{nd})}. \quad (14)$$

Using this expression, we plotted in Fig. 6 the disease severity as a function of the number of components in the mixture n . Panel (a) illustrates the case of a pathogen with the high rate of transmission and panel (b) shows the case a pathogen with the intermediate rate of transmission. The grey solid curves represent the homogeneous case when $\beta_{nd} = \beta_d > 0$, i. e. no specialization, every pathogen strain or species is equally likely to infect every host. Evidently, in this case the disease severity is independent of the number of mixture components. In all other cases considered in Fig. 6, the disease severity decreases with n . The black solid curves in Fig. 6 illustrate the case of full specialization, when $\beta_{nd} = 0$, $\beta_d > 0$. In this case, the disease severity decreases steeply with increasing n , eventually reaching zero. The dashed curves in Fig. 6 correspond to intermediate cases with different degrees of partial specialization. As the degree of host

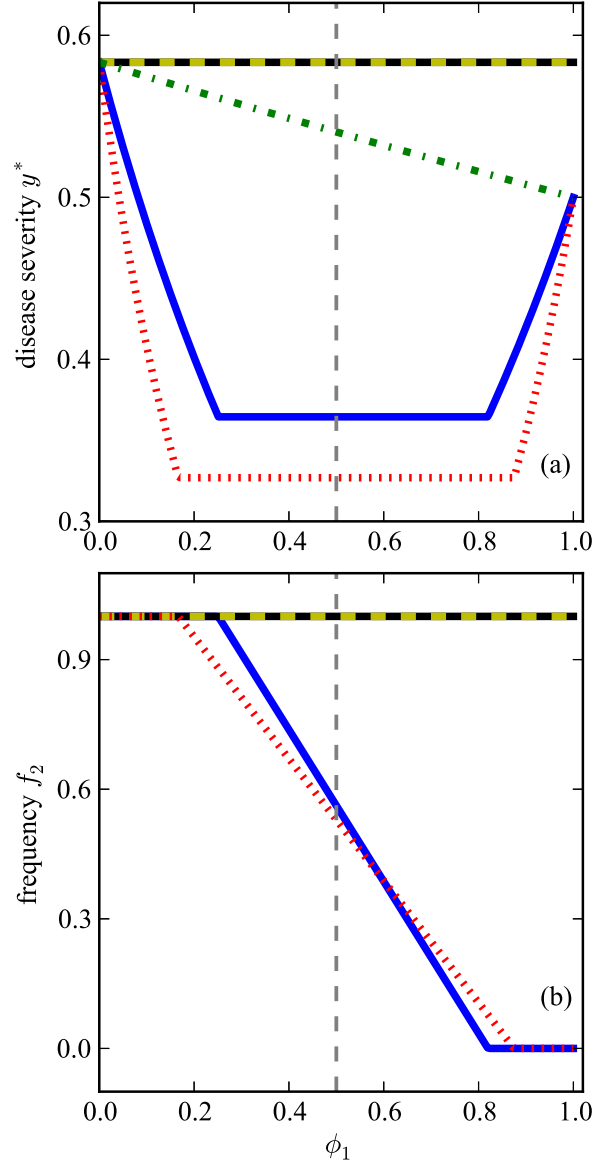


Figure 4: Disease severity y^* (upper panel) and the frequency $f_2^* = I_2^*/(I_1^* + I_2^*)$ of pathogen 2 (lower panel) at equilibrium as functions of the proportion of host 1 in the mixture $\phi_1 = K_1/(K_1 + K_2)$, according to Eqs. (A.16), (A.17). Parameter values: $\beta_{11} = 6$, $\beta_{22} = 8$, $K = K_1 + K_2 = 1$, $r = 0.2$, $\mu = 1$. The non-diagonal elements of the infection matrix \mathbf{B} determine the degree of specialization: (a) full specialization $\beta_{12} = \beta_{21} = 0$ (red dotted); (b) small degree of specialization $\beta_{12} = \beta_{21} = 0.9$ (blue, solid); (c) no specialization $\beta_{12} = \beta_{11} = 6$, $\beta_{21} = \beta_{22} = 8$ (black, upper); (d) strict gene-for-gene interaction $\beta_{21} = \beta_{22} = 8$, $\beta_{12} = 0$ (yellow, upper); (e) single pathogen $\beta_{11} = \beta_{21} = 6$, $\beta_{22} = \beta_{12} = 8$ (green, dash-dotted). Cases (c) and (d) correspond to the upper lines and overlap completely.

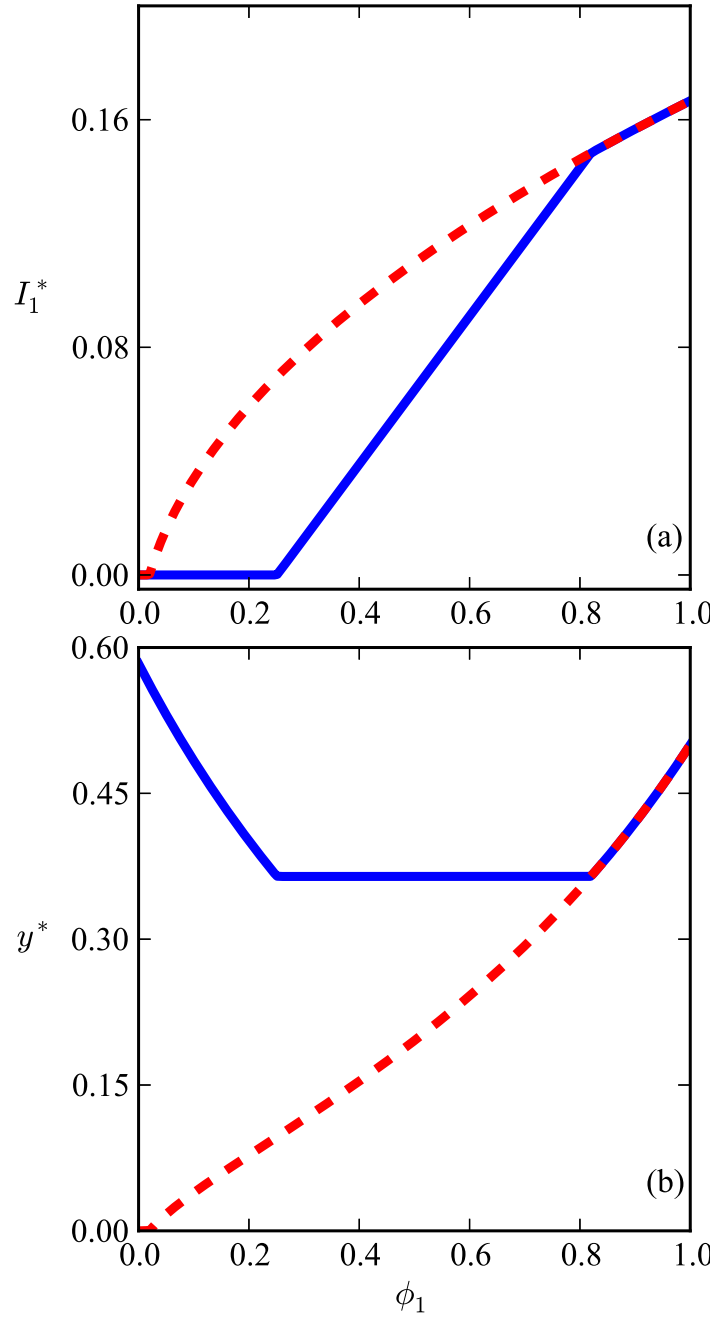


Figure 5: The effect of competition between the two pathogens P_1 and P_2 on the amount of disease. (a) I_1^* is plotted as a function of $\phi_1 = K_1/(K_1+K_2)$ at $\beta_{22} = \beta_{21} = 0$ (red, dashed curve), in which case P_2 is absent and no competition occurs; and at $\beta_{22} = 8, \beta_{21} = 0.9$ (blue, solid curve), when P_2 is present and competes with P_1 . (b) the disease severity y^* is plotted versus ϕ_1 at $\beta_{22} = \beta_{21} = 0$ (red, dashed curve) and at $\beta_{22} = 8, \beta_{21} = 0.9$ (blue, solid curve). Other parameter values are the same as in Fig. 4.

specialization increases, the decrease in disease severity becomes stronger.

Can one eradicate the disease by adding a large enough number of components to the host mixture? As we increase the number of components in the host mixture, each pathogen strain can infect less of its preferred host. At the limit of very large n , the amount of preferred host tissue available for each pathogen strain is so small that they are not able to survive only on it. Therefore, whether we can eradicate the disease depends on the ability of pathogen strains to survive on hosts that are not their favorite. This is determined by the parameter $R_{0\text{nd}} = \beta_{\text{nd}}K_{\text{tot}}/\mu$, which is the basic reproductive number of pathogen strains as a whole in the absence of their preferred hosts. If $R_{0\text{nd}} > 1$, then pathogen strains can survive in the absence of their preferred hosts. In this case, disease severity tends to a constant positive value at large n and never decreases to zero (dash-dotted curve in Fig. 6). In contrast, when $R_{0\text{nd}} < 1$, pathogen strains die out in the absence of their preferred hosts.

We take the limit of very large n in Eq. (14) and find that the disease severity is proportional to $R_{0\text{nd}} - 1$ in this case:

$$y_{\text{tot}}^*(n)_{n \rightarrow \infty} = r \frac{R_{0\text{nd}} - 1}{\mu + r(R_{0\text{nd}} - 1)}, \quad (15)$$

where

$$R_{0\text{nd}} = \beta_{\text{nd}}K_{\text{tot}}/\mu \quad (16)$$

is the basic reproductive number of pathogen strains overall in the absence of their preferred hosts. It follows from Eq. (A.36) that if $R_{0\text{nd}} \leq 1$, then the disease severity will eventually reach (or approach) zero as we increase n . However when $R_{0\text{nd}} > 1$, the disease severity will approach a constant positive value given by Eq. (A.36). This means that, by increasing the number of components in the mixture, we decrease (eventually to zero) the impact of host-specialized infections characterized by rate β_{d} . However, the impact of non-specialized infections characterized by β_{nd} remains unchanged with the corresponding severity given by Eq. (A.36).

From the expression for the disease severity in Eq. (14), one can determine the optimal number of components to use in the mixture. One way to do this is to define an economically acceptable disease severity, y_{acc} , (for example 5%), and then determine the number of components in the mixture that decrease the disease severity down to y_{acc} . This is done by solving Eq. (14) with respect to n . As a result, we obtain

$$n_{\text{opt1}} = rK_{\text{tot}} \frac{(\beta_{\text{d}} - \beta_{\text{nd}})(1 - y_{\text{acc}})}{\mu(r + y_{\text{acc}}(\mu - r)) - r\beta_{\text{nd}}K_{\text{tot}}(1 - y_{\text{acc}})}. \quad (17)$$

Here, n_{opt1} is the number of mixture components at which the disease severity y_{acc} is reached. This is illustrated in Fig. 6, where the horizontal dashed line corresponds to $y_{\text{acc}} = 5\%$. The values of n at which this line intersects with disease severity curves correspond to optimum n_{opt1} given by Eq. (17). The optimum shifts to larger values with decreasing degrees of specialization [e. g. from $n_{\text{opt1}} = 9$ for the solid curve corresponding to full specialization to $n_{\text{opt1}} = 16$ for the dashed curve representing partial specialization

in Fig. 6(a)].

Another way to determine an optimal number of mixture components uses the fact that $y^*(n)$ decreases with n , but also considers that the rate of this decrease (i.e. the derivative $\frac{dy^*(n)}{dn}$) decreases with n . Hence, the benefit of adding one more component to a mixture that already has n components decreases with increasing n . Because of this, the dependence $y^*(n)$ eventually saturates to a constant value given by Eq. (A.36). Therefore, one can define a minimum decrease in disease severity due to adding one more host variety to the mixture Δy_{\min} that is still economically plausible. The number of mixture components at this minimum is optimal, i.e. $n = n_{\text{opt2}}$. Mathematically, n_{opt2} can be found from the equation $y_{\text{tot}}^*(n_{\text{opt2}} - 1) - y_{\text{tot}}^*(n_{\text{opt2}}) = \Delta y_{\min}$, where $y_{\text{tot}}^*(n)$ is given by Eq. (14). The solution reads as

$$n_{\text{opt2}} = \frac{\sqrt{\Delta y} [\mu^2 - r(K_{\text{tot}}(2b_d - 3b_{\text{nd}}) + \mu)] + \sqrt{4(b_d - b_{\text{nd}})rK_{\text{tot}}\mu^2 + \Delta yC}}{2\sqrt{\Delta SC^2}}, \quad (18)$$

where

$$C = \mu^2 + r(b_{\text{nd}}K_{\text{tot}} - \mu). \quad (19)$$

This is also illustrated in Fig. 6, where the dotted vertical lines shows $n_{\text{opt2}} = 3$ [panel (a)] and $n_{\text{opt2}} = 2$ [panel (b)] that correspond to the severity curves for the case of strong partial specialization (dashed curves). When the degree of specialization is increased further up to full specialization (solid curve), n_{opt2} shifts to the larger value of four.

We expect mixtures to be more effective against pathogens with intermediate and low transmission [cf. panels (a) and (b) in Fig. 6]. In Fig. 6(b) a mixture with three components not only decreased the disease below the acceptable level [optimum number of components, according to Eq. (17)], but even eradicated the pathogen. A two-component mixture provided an economical optimum, according Eq. (18). In contrast, for pathogens with high transmission [Fig. 6(a)], mixtures with more components need to be used to reach the optimal effects.

The optimum number of components in the mixture, defined according to Eq. (17), can only be found if the acceptable severity y_{acc} can be reached by increasing n (that is when $R_{0\text{nd}} < 1$). This restriction is removed in the definition based on Eq. (18). But even in cases when y_{acc} can be reached by increasing n , the second definition seems to be more plausible, since it incorporates the economic costs of introducing an additional component into the mixture. However, it does not ensure that the disease will be reduced down to an acceptable value. Hence, additional disease control measures (e.g. applications of fungicides) may need to be implemented in order to further reduce the disease.

5. Discussion

We have shown that when a population of crop plants is exposed to two host-specialized pathogen strains or species, the overall severity of both diseases is smaller in the mixture of two host varieties than in either of the pure stands. We obtained analytical expressions

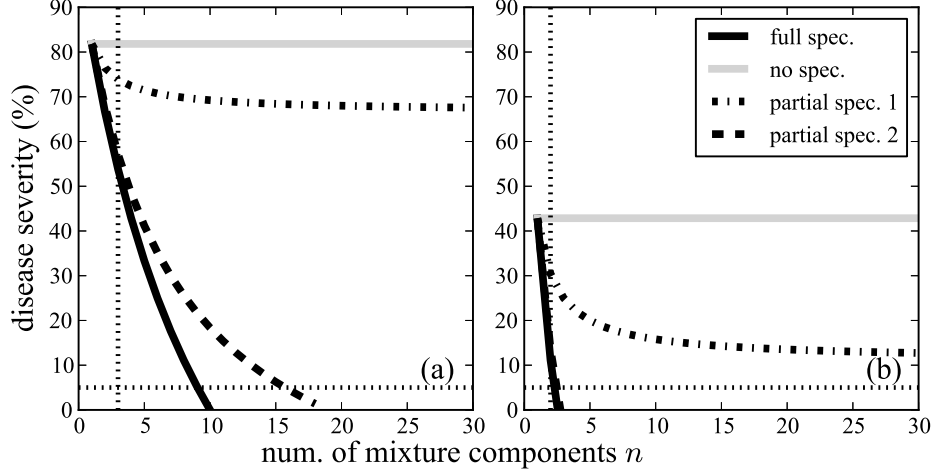


Figure 6: Disease severity at the infected equilibrium versus the number of components in the host mixture plotted according to Eq. (14) in the case of no specialization (grey solid), full specialization (solid), partial specialization with the specialization index $\sigma = \beta_{nd}/\beta_d = 0.5$ (dash-dotted) and $\sigma = 0.05$ (dashed). Parameter values: (a) pathogen with high transmission $\beta_d = 2$; (b) pathogen with low transmission $\beta_d = 0.5$. The rest of parameters are the same in (a) and (b): $K_{tot} = 1$, $\mu = 0.2$, $r = 0.1$. Dotted horizontal curve shows an example of a maximum disease severity, $S_{acc} = 5\%$, that is still economically acceptable. Dotted vertical lines show the optimal number of components $n_{opt2} = 3$ [panel (a)] and $n_{opt2} = 2$ [panel (b)], according to Eq. (18) taking $\Delta S = 10\%$, for the dashed curves.

for the disease reduction which allowed us to quantify it across the whole range of parameters. These findings may help to identify crop cultivars to be deployed in mixtures that will successfully control diseases prevalent in a given region. The overall disease severity can be minimized over a range of mixing ratios. The two pathogens coexist in this range and further adjusting the mixing ratio within this range makes it possible to control the relative abundance of each pathogen. This can be useful when one of the pathogens is less desirable, for example due to mycotoxin production or fungicide resistance, while a certain amount of the other pathogen can be tolerated. Alternatively, the mixing ratio can be adjusted within this optimal range to increase the economic output of the crop, if the two host varieties differ in their quality or commercial value.

We also generalized the model to describe host mixtures with more than two components. We find that when there is a degree of host specialization, the overall disease severity decreases with the number of components in the mixture. The more specialized the host-pathogen pairs are, the stronger is the decrease in the disease severity. Based on this understanding, we proposed ways to determine economically optimal numbers of components in host mixtures. Furthermore, this more general framework is capable of describing many hosts exposed to many pathogen strains or species and can also be used to better understand plant-pathogen dynamics in natural ecosystems, such as *Linum marginale*–*Melampsora lini* [58], or *Plantago lanceolata*–*Podosphaera plantaginis* [59]. Local adaptation was detected in these natural interactions [58, 59], hence the insight we gained in the case of partial specialization may advance our understanding of evolutionary forces operating in these wild plant-pathogen systems.

Four distinct mechanisms of disease reduction by host mixtures are described in the literature [32, 23, 34]: (i) the effect of reduced density of susceptibles; (ii) the “barrier effect”; (iii) induced resistance; and (iv) competition between pathogens. In scenario (i) the disease is reduced in the mixture simply because it has less of the susceptible variety than the susceptible pure stand. This “reduced density” effect can be observed most clearly by comparing the amount of disease in two pure stands of the susceptible variety, which differ only in planting density [32]. The introduction of the resistant variety further reduces the disease in the mixture (scenario (ii)), because the transmission between susceptible hosts is hindered (a resistant “barrier” is created between adjacent susceptible plants). Induced resistance (scenario (iii)) takes place when spores of an avirulent pathogen activate a host resistance mechanism that is also effective against another pathogen (or another race of the same pathogen), which is normally able to infect the host [32, 41, 61]. Finally, in scenario (iv) mixing host cultivars is expected to make the pathogens compete with each other for host tissue [34, 46].

The “reduced density” effect originally referred to the mixture of a susceptible and a resistant variety [32]. Hence, it cannot lead to a disease level lower than in the pure stand of the resistant variety. Here we extended the notion of the “reduced density” effect to the case of two or more host-specialized pathogen strains or species. For example, this may correspond to host 1 being susceptible to pathogen 1, but resistant to pathogen 2 and host 2 being susceptible to pathogen 2, but resistant to pathogen 1. We find that it is only in such cases that disease level in the mixture is lower than in both pure stands.

Our results also indicate that although the presence of the second pathogen may

suppress the population of the first one, the overall disease severity due to both of them increases (Fig. 5). Hence, according to our model, the competition between pathogens (scenario (iv)) alters the relative abundance of each of them, but is not capable of reducing the overall disease severity.

Our model does not include the “barrier” effect, since it does not explicitly consider the spatial dependence of pathogen dispersal (see Sec. 2). Also, induced resistance [32, 41, 61] was not considered. Therefore, we likely underestimate the effect of host mixtures on disease reduction. However, the model can be readily extended to include both of these effects. In this way, a unified mathematical framework for description of the effect of host mixtures on plant disease can be developed on the basis of the model presented here. This would allow one to better understand the relative contributions of each of these effects in disease reduction and design better host mixtures.

Here we focused on the benefit host mixtures may provide in terms of reduction of disease. But how do host mixtures influence pathogen evolution over longer time scales? To investigate the durability of resistance in the context considered here, when a mixture of two host varieties is exposed to two different pathogens (or different races of the same pathogen), each specialized on one of the host varieties, one needs to first consider the likelihood of emergence of a third pathogen race, which can infect both host varieties equally successfully (the “super-race”), but might bear a fitness cost associated with the extended host range. In this scenario, the conditions under which this pathogen race will be favored by selection need to be considered. This can be done by using mathematical frameworks similar to the ones developed in [62, 47] and is a promising direction for future study.

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A. Electronic Supplementary Material

A.1. Fixed points of the two hosts–two pathogens model

The system of equations (1)-(4) has six fixed points:

FP1: $H_1^* = K_1, H_2^* = K_2, I_1^* = I_2^* = 0$; both pathogens die out

FP2: $H_1^* \neq 0, H_2^* \neq 0, I_1^* \neq 0, I_2^* = 0$; P_1 wins

FP3: $H_1^* \neq 0, H_2^* \neq 0, I_1^* \neq 0, I_2^* = 0$; P_1 wins

FP4: $H_1^* \neq 0, H_2^* \neq 0, I_1^* \neq 0, I_2^* \neq 0$; P_1, P_2 coexist

FP5: $H_1^* \neq 0, H_2^* \neq 0, I_1^* = 0, I_2^* \neq 0$; P_2 wins

FP6: $H_1^* \neq 0, H_2^* \neq 0, I_1^* = 0, I_2^* \neq 0$; P_2 wins

Over the whole range of biologically plausible parameter values ($r > 0$; $K_1 > 0$; $K_2 > 0$; $\beta_{ij} \geq 0, i, j = 1..2$; $\mu > 0$), only four of the fixed points (we denote them as FP1, FP2, FP4, FP5) correspond to positive values of the corresponding amounts of host tissue $H_1^*, H_2^*, I_1^*, I_2^*$, while the fixed points FP3 and FP6 correspond to at least one of the quantities $H_1^*, H_2^*, I_1^*, I_2^*$ being negative, which is biologically unrealistic. We are interested in the case when at least one of the pathogens survives. Therefore, we consider the expressions for $H_1^*, H_2^*, I_1^*, I_2^*$ at the fixed points FP2, FP4, FP5.

Values of I_1, I_2, H_1 and H_2 at the fixed point FP2 are given by

$$I_{1\{\text{FP2}\}} = r \frac{\beta_{11}\beta_{12}K - \mu_1(\beta_{11} + \beta_{12}) + \sqrt{B_{\text{FP2}}}}{2\beta_{11}\beta_{12}\mu_1}, \quad I_{2\{\text{FP2}\}} = 0, \quad (\text{A.1})$$

$$H_{1\{\text{FP2}\}} = \frac{-\beta_{11}\beta_{12}K + \mu_1(\beta_{11} - \beta_{12}) + \sqrt{B_{\text{FP2}}}}{2\beta_{11}(\beta_{11} - \beta_{12})}, \quad (\text{A.2})$$

$$H_{2\{\text{FP2}\}} = \frac{\beta_{11}\beta_{12}K + \mu_1(\beta_{11} - \beta_{12}) - \sqrt{B_{\text{FP2}}}}{2\beta_{12}(\beta_{11} - \beta_{12})}, \quad (\text{A.3})$$

where

$$B_{\text{FP2}} = 4\beta_{11}\beta_{12}(\beta_{11} - \beta_{12})\mu_1\phi_1K + [\beta_{11}\beta_{12}K - (\beta_{11} - \beta_{12})\mu_1]^2. \quad (\text{A.4})$$

Values of I_1, I_2, H_1 and H_2 at the fixed point FP5 are given by

$$I_{2\{\text{FP5}\}} = r \frac{\beta_{22}\beta_{21}K - \mu_2(\beta_{22} + \beta_{21}) + \sqrt{B_{\text{FP5}}}}{2\beta_{22}\beta_{21}\mu_2}, \quad I_{1\{\text{FP5}\}} = 0, \quad (\text{A.5})$$

$$H_{1\{\text{FP5}\}} = \frac{\beta_{22}\beta_{21}K + \mu_2(\beta_{22} - \beta_{21}) - \sqrt{B_{\text{FP5}}}}{2\beta_{21}(\beta_{22} - \beta_{21})}, \quad (\text{A.6})$$

$$H_{2\{\text{FP5}\}} = \frac{-\beta_{22}\beta_{21}K + \mu_2(\beta_{22} - \beta_{21}) + \sqrt{B_{\text{FP5}}}}{2\beta_{22}(\beta_{22} - \beta_{21})}, \quad (\text{A.7})$$

where

$$B_{\text{FP5}} = -4\mu_2\phi_1K\beta_{22}\beta_{21}(\beta_{22} - \beta_{21}) + [\beta_{22}\beta_{21}K + \mu_2(\beta_{22} - \beta_{21})]^2. \quad (\text{A.8})$$

Values of I_1 , I_2 , H_1 and H_2 at the fixed point FP4 are given by

$$I_{1\{\text{FP4}\}} = r \frac{\beta_{22}\beta_{21}\mu_1 (C_{21}\mu_1 - KC_-) + [(\phi_1 C_- + \beta_{12}\beta_{21})C_- K - C_{21}C_+\mu_1] \mu_2 + \beta_{12}\beta_{21}C_{21}\mu_2^2}{C_- (\beta_{21}\mu_1 - \beta_{11}\mu_2)(\beta_{12}\mu_2 - \beta_{22}\mu_1)}, \quad (\text{A.9})$$

$$I_{2\{\text{FP4}\}} = r \frac{(\beta_{22}\mu_1 - \beta_{12}\mu_2) [\beta_{11}C_- K - C_{12}(\beta_{11}\mu_2 - \beta_{21}\mu_1)] - C_-^2 \phi_1 K \mu_1}{C_- (\beta_{11}\mu_2 - \beta_{21}\mu_1)(\beta_{22}\mu_1 - \beta_{12}\mu_2)}, \quad (\text{A.10})$$

$$H_{1\{\text{FP4}\}} = \frac{\beta_{22}\mu_1 - \beta_{12}\mu_2}{\beta_{11}\beta_{22} - \beta_{12}\beta_{21}}, \quad (\text{A.11})$$

$$H_{2\{\text{FP4}\}} = \frac{\beta_{11}\mu_2 - \beta_{21}\mu_1}{\beta_{11}\beta_{22} - \beta_{12}\beta_{21}}, \quad (\text{A.12})$$

where

$$C_{12} = \beta_{11} - \beta_{12}, \quad C_{21} = \beta_{22} - \beta_{21} \quad (\text{A.13})$$

$$C_- = \beta_{11}\beta_{22} - \beta_{12}\beta_{21}, \quad (\text{A.14})$$

$$C_+ = \beta_{11}\beta_{22} + \beta_{12}\beta_{21}. \quad (\text{A.15})$$

Next, we can obtain the expressions for the disease severity

$$y^* = \frac{I_1^* + I_2^*}{I_1^* + I_2^* + H_1^* + H_2^*} \quad (\text{A.16})$$

and for the frequency of pathogen 2 at equilibrium

$$f_2^* = \frac{I_2^*}{I_1^* + I_2^*} \quad (\text{A.17})$$

corresponding to different fixed points described above. Since we consider only two pathogens, the frequency of the pathogen 1 at equilibrium is then $f_1^* = 1 - f_2^*$.

In order to determine the dependence of y^* and f_2^* on the proportion of host variety 1 in the mixture ϕ_1 and the fungicide concentration C , we choose from the expressions (A.1)-(A.11) those which correspond to a stable fixed point at a given value of ϕ_1 and C , and substitute them in Eq.(A.16) and Eq.(A.17). The result of this procedure is shown in Fig. 4.

A.2. Linear stability of the fixed points and invasion thresholds for the two hosts–two pathogens model

The trivial fixed point FP1 (both pathogens die out) is realized when both $R_{01} < 1$ and $R_{02} < 1$, where

$$R_{01} = (\beta_{11}K_1 + \beta_{12}K_2)/\mu, \quad (\text{A.18})$$

$$R_{02} = (\beta_{21}K_1 + \beta_{22}K_2)/\mu, \quad (\text{A.19})$$

That is when $\beta_{11} < \beta_{11b}$ and $\beta_{22} < \beta_{22b}$, where

$$\beta_{11b} = (\mu - K_2\beta_{12})/K_1, \quad (\text{A.20})$$

$$\beta_{22b} = (\mu - K_1\beta_{21})/K_2. \quad (\text{A.21})$$

If $\beta_{11} > \beta_{11b}$, but $\beta_{22} < \beta_{22b}$, then the pathogen P_1 wins. And vice versa, if $\beta_{22} > \beta_{22b}$, but $\beta_{11} < \beta_{11b}$, then the pathogen P_2 wins.

Now, we determine the threshold for invasion of the pathogen P_2 , when the host population is already infected at equilibrium with the pathogen 1 (this corresponds to the fixed point FP2). We linearize the system (1)-(4) in the vicinity of the fixed point FP2 and search for the conditions under which it becomes unstable with respect to the invasion of P_2 . In order to do this, we only need to consider the linearized equation for I_2 , since it becomes uncoupled from the other equations:

$$\frac{dI_2}{dt} = \lambda_2 I_2, \quad (\text{A.22})$$

where

$$\lambda_2 = \beta_{21}H_{1\{FP2\}}^* + \beta_{22}H_{2\{FP2\}}^* - \mu \quad (\text{A.23})$$

is the growth rate. Then, we obtain the corresponding basic reproductive number

$$R_{02\{FP2\}} = (\beta_{21}H_{1\{FP2\}}^* + \beta_{22}H_{2\{FP2\}}^*) / \mu. \quad (\text{A.24})$$

Here, the equilibrium values of the susceptible host density $H_{1\{FP2\}}^*$ and $H_{2\{FP2\}}^*$ are given by Eq. (A.3) and Eq. (A.3).

From Eq. (A.28) we obtain threshold value of the transmission rate, above which the pathogen 2 can invade:

$$b_{22c} = \frac{\beta_{12}(\beta_{12}\beta_{21}K + [2(\beta_{11} - \beta_{12}) - \beta_{21} + \beta_{12}\beta_{21}/\beta_{11}]\mu - \beta_{21}/\beta_{11}\sqrt{B_{FP2}})}{(\beta_{11} - \beta_{12})\mu + \beta_{11}\beta_{12}K - \sqrt{B_{FP2}}}, \quad (\text{A.25})$$

where B_{FP2} is given by Eq. (A.4).

Similarly, we determine the threshold for invasion of pathogen 1 (I_1), when the host population is already infected at equilibrium with pathogen 2 (this corresponds to the fixed point FP5). Again, we linearize the system (1)-(4) in the vicinity of the fixed point FP5 and search for the conditions under which it becomes unstable with respect to the invasion of pathogen 1. In order to do this, we only need to consider the linearized equation for I_1 , since it becomes uncoupled from other equations:

$$\frac{dI_1}{dt} = \lambda_1 I_1, \quad (\text{A.26})$$

where

$$\lambda_1 = \beta_{11}H_{1\{FP5\}}^* + \beta_{12}H_{2\{FP5\}}^* - \mu \quad (\text{A.27})$$

is the growth rate. Then, we obtain the corresponding basic reproductive number

$$R_{01\{FP5\}} = (\beta_{11}H_{1\{FP5\}}^* + \beta_{12}H_{2\{FP5\}}^*) / \mu. \quad (\text{A.28})$$

Here, the equilibrium values of the susceptible host density $H_{1\{FP5\}}^*$ and $H_{2\{FP5\}}^*$ are given by Eq. (A.6) and Eq. (A.7).

Similarly the critical value of the infection rate b_{11c} , above which the pathogen 2 can invade, reads

$$b_{11c} = \frac{\beta_{21}(\beta_{21}\beta_{12}K + [2(\beta_{22} - \beta_{21}) - \beta_{12} + \beta_{21}\beta_{12}/\beta_{22}]\mu - \beta_{12}/\beta_{22}\sqrt{B_{FP5}})}{(\beta_{22} - \beta_{21})\mu + \beta_{22}\beta_{21}K - \sqrt{B_{FP5}}}, \quad (\text{A.29})$$

where B_{FP5} is given by Eq. (A.8).

A.3. Disease severity when n hosts are exposed to n pathogens

Consider the case when n hosts are exposed to n pathogens and the transmission matrix has a simple form given by Eq. (11), where every diagonal element of the matrix \mathbf{B} is equal to β_d and every non-diagonal element is β_{nd} . We assume that every host variety is planted at the same proportion, i. e. $K_i = K$. In addition, we assume that all healthy and infected hosts start with the same initial conditions. Hence, their dynamics are the same and is described by a simplified system of Eqs. (12)-(13)

$$\frac{dH_p}{dt} = r(K - H_p) - \beta_{\text{eff}}I_pH_p, \quad (\text{A.30})$$

$$\frac{dI_p}{dt} = \beta_{\text{eff}}I_pH_p - \mu I_p, \quad (\text{A.31})$$

where $\beta_{\text{eff}} = \beta_d + (n-1)\beta_{nd}$. Then, the values of host densities at the infected equilibrium read:

$$H_p^* = \frac{\mu}{\beta_{\text{eff}}}, \quad I_p^* = \frac{rK}{\mu} \left(1 - \frac{\mu}{\beta_{\text{eff}}K} \right). \quad (\text{A.32})$$

The total amounts of healthy and infected hosts are again obtained by multiplying H_p and I_p by n :

$$H_{\text{tot}}^* = nH_p^* = \frac{n\mu}{\beta_d + (n-1)\beta_{nd}}, \quad (\text{A.33})$$

$$I_{\text{tot}}^* = nI_p^* = \frac{rK_{\text{tot}}}{\mu} \left(1 - \frac{n\mu}{(\beta_d + (n-1)\beta_{nd})K_{\text{tot}}} \right). \quad (\text{A.34})$$

In this case, the total disease severity at the infected equilibrium reads, according to Eq. (10):

$$y_{\text{tot}}^*(n) = r \frac{(\beta_{\text{d}} + (n-1)\beta_{\text{nd}}) K_{\text{tot}} - \mu n}{n\mu(\mu - r) + rK_{\text{tot}}(\beta_{\text{d}} + (n-1)\beta_{\text{nd}})}. \quad (\text{A.35})$$

Next, we take the limit of very large n in Eq. (14), which yields

$$y_{\text{tot}}^*(n)_{n \rightarrow \infty} = r \frac{R_{0\text{nd}} - 1}{\mu + r(R_{0\text{nd}} - 1)}, \quad (\text{A.36})$$

where

$$R_{0\text{nd}} = b_{\text{nd}} K_{\text{tot}} / \mu \quad (\text{A.37})$$

is the basic reproductive number of pathogen strains as a whole in the absence of their preferred hosts.